Occupational Risk Factors for Brain Tumors Among Women in Shanghai, China

Ellen F. Heineman, PhD Yu-Tang Gao, MD Mustafa Dosemeci, PhD Joseph K. McLaughlin, PhD

The etiology of brain cancer is not well understood and few studies have evaluated occupational risk factors among women. We evaluated occupation and industry at time of diagnosis for 276 incident primary brain tumor cases among women in Shanghai, China, for the period 1980-1984, identified through the Shanghai Cancer Registry. Standardized incidence ratios (SIRs) and their 95% confidence intervals (CIs) were calculated for all occupations and industries with at least three female cases. SIRs compared observed to expected numbers of cases, based on incidence rates for Shanghai and the number of women in each occupation and industry according to the 1982 census. Statistically significant excesses of brain tumors were seen among grain farmers (SIR = 6.5, 95% CI = 1.3-19.1), rubber workers (SIR = 5.0, 95%)CI = 1.6-11.6), and workers in transportation equipment manufacture and repair (SIR = 2.3, 95% CI = 1.1-4.3). Risks among textile spinners and winders were of borderline significance (SIR = 1.7, 95% CI = 1.0-2.8). Elevated but nonsignificant risks of 2.0 or greater were seen among nurses, plastic products workers, sanitation workers, painters, and workers in manufacture of equipment for electrical generation, transmission, and distribution. Results for farmers, rubber workers, and painters are consistent with previously reported excesses among these occupations in men. The increase among nurses is a new finding, although elevated risks have been observed among male medical professionals. Risks were elevated with likely exposure to pesticides, particularly among those thought to have a high probability and a high level of exposure (SIR = 3.6, 95% CI = 1.2-8.5).

From the Epidemiology and Biostatistics Program, Division of Cancer Epidemiology, National Cancer Institute, Rockville, Maryland (Dr Heineman, Dr Dosemeci, Dr McLaughlin) and the Department of Epidemiology, Shanghai Cancer Institute, Shanghai, China (Dr Gao).

Address correspondence to: Ellen F. Heineman, PhD, Occupational Studies Section, National Cancer Institute, 6130 Executive Blvd, Room 418, Rockville, MD 20852.

1076-2752/95/3703-0288\$3.00/0

Copyright © by American College of Occupational and Environmental Medicine

he incidence and mortality of brain tumors have been increasing in Shanghai over the past two decades. Some of this increase may be due to improvements in diagnosis; it is unclear how much represents true changes in rates. In Shanghai, rates of brain tumors overall in women and men are similar. However, as in other countries, women have higher proportions of benign or noninvasive tumors.

The etiology of brain tumors is not well understood. Few studies have included women or reported on occupational risk factors for either malignant or benign brain tumors among women. Excess risks among men have been reported for a variety. of industries and occupations, but in most studies, specific substances that increase risk have not been identified. To evaluate occupational factors among women, we compared employment data for cases of brain tumor diagnosed in Shanghai, China, with census information on the occupation for the urban population of Shanghai.

Methods

Shanghai is the largest industrial city in China. Its cancer registry, established in 1963, is the oldest population-based cancer registry in the country. Details of the collection and linkage of the cancer registry and census data have been published previously.^{3,4} Briefly, the registry includes all incident cases of cancer and nonmalignant brain tumors diagnosed in the 10 urban districts of Shanghai. Registry personnel obtained information on the occupation

and industry at the time of diagnosis from cases themselves, their next of kin, or their work supervisors, for over 98% of cases.^{3,4} Included in this study are the 276 incident primary brain tumor cases diagnosed among women aged 30 or older in urban Shanghai, China, in 1980–1984 and identified through the Shanghai Cancer Registry.

The observed number of cases was compared to the expected number of incident brain tumors for each occupation and industry. Expected numbers were calculated by applying age-specific incidence rates for 1980-1984 from the Shanghai Cancer Registry to the number of women in each occupation and industry, based on data from the 1982 census (the midpoint of the case ascertainment period) and a survey of retirees from the same 10 urban districts. Occupation and industry had been recorded on the census form and coded using a standardized Chinese code system with up to 300 specific occupations and 200 specific industries for women who were working at the time of the census. For retirees, a special survey was made of a 10% sample to determine occupation and industry at retirement.3,4 Accuracy of the occupational reports was evaluated by comparison of occupational data on cases from the registry with occupational data obtained in the census. For women, concordance was over 95% for broad industry or occupation classification and over 85% for the most narrow occupational groups.3

An industrial hygienist (MD) with experience in industrial settings in China assessed the probability of exposure (none, low, high) and level of exposure (low, high) for four agents, based on occupation. Assessments were done without knowledge of the distribution of cases' occupations. The exposures were organic solvents, benzene, pesticides, and electromagnetic fields (EMFs). For each exposure, observed and expected numbers were summed for all occu-

pations considered to entail that probability or level of exposure.

Standardized incidence ratios (SIRs) and 95% confidence intervals (CIs) were calculated for all occupations and industries with at least three female cases and for the four exposures.

Results

For occupation (Table 1), statistically significant excesses of brain tumors were seen among grain farmers and rubber workers. Risks among textile workers were of borderline significance and reflected increases in several specific occupations, including spinners and winders, weavers, and other textile workers. Twoto threefold elevated risks were observed among nurses, sanitation workers, plastic products workers, and painters, but none was statistically significant.

For industry (Table 2), only workers employed in transportation equipment manufacture and repair had a statistically significant (twofold) excess of brain tumors. The risk elevation appeared in both subsets of the industry, motor vehicle manufacture and shipbuilding. A risk elevation in grain production was of borderline significance. Risk were twofold or greater in the rubber industry; in manufacture of equipment for electrical generation, transmission and distribution; in public utilities; and in sanitation services, but here they were not statistically significant.

Risks were significantly elevated in occupations thought to entail exposure to organic solvents (Table 3). Risks rose with probability and level of exposure to organic solvents to nearly twofold among women thought to have both high probability and high level of exposure. Benzene showed a similar pattern, but the number of exposed cases was small in all but the high-probability/high-level group. The apparent increases in risk of brain tumor with probability and level were driven primarily by that high/high group. There

was considerable overlap between the benzene-exposed and organic solvent-exposed groups. Two-thirds (16 of 24) of the women who were considered probably exposed to high levels of organic solvents were also considered to have high probability and high level of exposure to benzene.

Risks were elevated with likely exposure to pesticides, rising to over threefold among women considered to have high probability and level of exposure (Table 3). Cases in this exposure category were three grain farmers, a grain miller, and a woman employed in forest development and tree farming. There were no cases in the intermediate (low probability/ high level or high probability/low level) exposure groups. Potential exposure to EMFs showed little evidence of an association with brain tumors; risk did not increase with probability or level of exposure.

Discussion

We observed statistically significant excesses of brain tumors among grain farmers, rubber workers, and workers employed in transportation equipment manufacture and repair, and with likely exposure to pesticides, particularly those workers thought to have high probability and high level of exposure. Elevated but nonsignificant risks were also seen among nurses, sanitation workers, plastic products workers, and painters, and among women employed in electrical equipment manufacture and in public utilities. Because of the large number of comparisons, some observed associations may be due to chance. However, many are similar to findings of previous studies.

Excesses for farmers are consistent with previous studies, chiefly among men.^{5,6} Two studies that found elevated risks for malignant brain tumors among Italian farmers included woman.^{7,8} Two other studies reported data for women separately; neither found increased risks for female farmers.^{9,10} Increased risks among Shanghai women who

TABLE 1
Standardized Incidence Ratios for Risk of Brain Cancer for Occupation Among Women in Shanghai, China*

Occupation	Cases (n = 276)	Standardized Incidence Ratio	95% Confidence Interval
Professional and technical workers	25	0.8	(0.5–1.2)
Nurses	5	2.4	(0.8-5.7)
Economists, financial planners	6	0.7	(0.3–1.5)
Accountants and bookkeepers	3	0.6	(0.1-1.6)
Teachers	10	1.0	(0.5–1.9)
Middle school and technical school	3	0.9	(0.2–2.7)
Primary school	. 6	1.4	(0.5–3.1)
Leaders of government agencies, parties, mass organizations and businesses	3	0.5	(0.1–1.5)
Clerical and related	7	0.9	(0.4-2.0)
Administrative clerks	6	1.1	(0.4–2.5)
Sales workers	7	0.6	(0.2–1.3)
Service	32	1.0	(0.7–1.5)
Public service workers	22	0.9	(0.6-1.4)
Sanitation workers, street cleaners, garbage handlers	3	2.7	(0.6-7.9)
Cooks	9	1.3	(0.6–2.4)
Agriculture, forest, fishers, hunters	4	2.8	(0.8–7.2)
Farmers	3	2.8	(0.6–8.0)
Grain farmers	3	6.5	(1.3–19.1)
Production, transportation, and related workers	139	1.2	(1.0–1.4)
Metal refining and processing workers	5	1.6	(0.5–3.8)
Rubber and plastic product makers	10	2.4	(1.2-4.5)
Rubber and products manufacturing workers	5	5.0	(1.6–11.6)
Rubber and products manufacturing workers, except tires	4	4.4	(1.2–11.3)
Plastic	5	2.3	(1.2–4.5) (1.6–11.6) (1.2–11.3) (0.8–5.5)
Textile workers	40	1.4	(1.0–1.9)
Fiber preparers, spinners and winders, weavers, knitters	36	1.4	(1.0–1.9)
Spinners and winders	16	1.7	(1.0-2.8)
Weavers	17	1.6	(0.9–2.5)
Knitters	3	0.7	(0.2–2.2)
Other textile workers	3	2.1	(0.46.1)
Tailors	12	1.2	(0.6–2.2)
Tailors and sewers	8	1.3	(0.6–2.6)
Food and beverage processors	3	1.6	(0.3-4.7)
Pulp and paper products makers	6	1.5	(0.5–3.2)
Paper products makers	5	1.4	(0.5–3.3)
Printers and related workers	3	1.6	(0.3-4.6)
Blacksmiths, toolmakers, machine-tool operators	13	1.3	(0.7–2.2)
Metal grinders, polishers, tool sharpeners, and machine-tool operators	8	1.4	(0.6–2.8)
Other blacksmiths, toolmakers	4	1.2	(0.3-3.1)
Electric and electronics workers	6	0.7	(0.3–1.5)
Electric and electronic equipment assembly workers	4	0.8	(0.2–1.9)
Plumbers, welders, sheet metal, and structural metal erectors	4	1.2	(0.3–3.0)
Painters	4	3.0	(0.8-7.8)
Other production and related workers	3	0.6	(0.1–1.8)
Material handlers, dockers, freight handlers	3	0.9	(0.2–2.5)
Inspectors and product analyzers	6	0.8	(0.3–1.8)
Quality inspectors	4	0.7	(0.2–1.7)
Other transportation/production workers	10	1.1	(0.5–2.0)
Packaging workers	7	1.4	(0.6-3.0)
Warehouse workers	3	0.7	(0.1–2.0)

^{*} Occupations with at least three female cases. Ratios adjusted for age.

TABLE 2
Standardized Incidence Ratios for Risk of Brain Cancer for Industry Among Women in Shanghai, China*

industry	Cases (n = 276)	Standardized Incidence Ratio	95% Confidence Interval
Agriculture	4	2.8	(0.8–7.3)
Grain production	3	4.7	(1.0–13.7)
Manufacturing	158	1.1	(0.9–1.3)
Food products	5	1.4	(0.5-3.3)
Textile mill products	48	1.2	(0.9-1.5)
Cotton spinning, weaving and dyeing	33	1.2	(0.9-1.7)
Wool spinning, weaving and dyeing	6	1.5	(0.6-3.3)
Knitting mills	5	0.7	(0.2–1.5)
Apparel and other textile products	11	1.3	(0.6-2.2)
Apparel products	8	1.2	(0.5-2.4)
Paper and allied products	7	1.4	(0.6-2.8)
Paper processing	5	1.2	(0.4–2.7)
Stationery, musical instruments, crafts, sporting goods, and printing	7	0.8	(0.3–1.6)
Industrial crafts, metal, and hemp	4	1.0	(0.3-2.7)
Rubber and plastic products	11	1.8	(0.9–3.3)
Rubber and plastic products	5	2.4	(0.8–5.6)
Plastic	6	1.5	(0.6-3.4)
Nonmetallic mineral products, except insulating materials	3	1.2	(0.2–3.5)
Metallurgy	5	1.7	(0.5–3.9)
Black metal (blast furnace)	3	1.4	(0.3-4.0)
Fabricated metal products	9	0.9	(0.4–1.8)
Hardware (keys, knives)	3	0.6	(0.1–1.7)
Machinery	13	1.0	(0.5–1.7)
Special industry machinery	6	1.7	(0.6–3.6)
General industrial machinery	3	1.8	(0.4–5.2)
Electric and electronic machinery	18	1.0	(0.6–1.5)
•	4	2.2	(0.6–5.5)
Electric generation, transmission, distribution, and equipment			
Miscellaneous electrical equipment (lighting, wiring)	7	1.3	(0.5–2.7)
Transportation and repair	10	2.3	(1.1–4.3)
Motor vehicles, accessories, and repair	6	2.3	(0.9–5.1)
Shipbuilding and repair	4	3.0	(0.8–7.8)
Precision machinery, instruments and meters	5	0.8	(0.2–1.8)
Transportation, postal, communication	3	0.5	(0.1–1.5)
Transportation	3	0.6	(0.1–1.7)
Trucking and bus	3	1.0	(0.2–3.0)
Commercial trade, restaurant and goods supply, and marketing services	23	1.1	(0.7–1.6)
Domestic trade	12	0.8	(0.4-1.4)
Eating and drinking places	5	1.2	(0.4–2.7)
Housing, public utilities administration, personal services	7	0.8	(0.3–1.7)
Public utilities services	4	2.2	(0.6–5.6)
Sanitation services	3	2.2	(0.4–6.4)
Health, athletic, social welfare services	. 6	0.8	(0.3–1.7)
Health services	6	1.0	(0.4–2.2)
Hospitals	6	1.2	(0.4–2.6)
Education, culture, and art	10	0.7	(0.3–1.2)
Education	10	0.7	(0.3-1.3)
Primary education	6	1.1	(0.4-2.5)
Middle education	3	0.7	(0.1–2.0)
Government agencies, parties, and mass organizations	3	0.5	(0.1–1.5)
Housewives	50	0.8	(0.6–1.1)

^{*} Industries with at least three female cases. Incidence ratios adjusted for age.

TABLE 3Age-adjusted Standardized Incidence Ratios for Risk of Brain Cancer for Specific Substances Among Women in Shanghai, China

Substance	Cases (n = 276)	Standardized Incidence Ratio	95% Confidence Interval
Organic solvents	116	1.3	(1.1–1.6)
Probability			
Low	89	1.2	(1.0–1.5)
High	27	2.0	(1.3-3.0)
Level			
Low	68	1.2	(1.0-1.6)
High	48	1.5	(1.1-2.0)
Probable exposure, high level	24	1.9	(1.2–2.8)
Benzene	24	1.7	(1.1–2.6)
Probability			
Low	5	1.6	(0.5-3.7)
High	19	1.8	(1.1–2.8)
Level			
Low	6	1.5	(0.6-3.4)
High	18	1.8	(1.1–2.9)
Probable exposure, high level	16	1.7	(1.0–2.8)
Pesticides	8	2.6	(1.3–6.0)
Probability			
Low	3	2.4	(0.5–7.1)
High	5	3.6	(1.2-8.3)
Level			
Low	3	2.4	(0.5–7.0)
High	5	3.6	(1.2-8.5)
Probable exposure, high level	5	3.6	(1.2–8.5)
Electromagnetic fields	82	1.2	(0.9–1.5)
Probability	70	4.0	(4.0.4.5)
Low	72	1.2	(1.0–1.5)
High	10	1.0	(0.5–1.8)
Level	70	4.0	(0.0.4.5)
Low	73	1.2	(0.9–1.5)
High	9	1.2	(0.5–2.2)
Probable exposure, high level	9	1.2	(0.6–2.3)

were considered to be exposed to pesticides are consistent with the suggestion that occupational exposure to pesticides may be partly responsible for excesses among farmers. 5-8

Results for rubber workers, plastic workers, and painters support previous reports among men.¹¹ An increased risk for brain tumors was recently reported for men and women painters combined.⁹

Previous studies have suggested that organic solvents are associated with brain tumors, particularly gliomas. 11-15 Our results provide supporting evidence for that hypothesis. Risks also appeared to increase with probability and level of benzene ex-

posure in these data. No previous studies, however, have provided evidence of an association of benzene with brain tumors. The association we observed may be confounded by exposure to other solvents, particularly because the association with the general class of solvents was about the same magnitude as that observed with benzene. Solvents, including benzene, may be partly responsible for the excesses observed in painters and rubber workers, but both occupations entail complex exposures. Additional detailed, exposure-specific analyses are needed to determine the agents responsible for these excesses.

Two other suggestive leads emerged from this study. First, although the twofold risk observed among nurses was not statistically significant, another recent study reported a similar finding.16 Two studies have reported significantly increased risks for glioma among women physicians¹⁷ and dental nurses. 18 Elevated risks have also been observed among male medical professionals. 17-19 Second, Shanghai women in wool spinning, weaving, and dyeing experienced a 50% excess of brain tumors. This could be due to chance, but also echoes a more than twofold significant association of work in the wool industry with brain cancer in Swedish women.17

Reports on EMFs and brain tumors are inconsistent. 20,21 We did not observe an association, but the number of women considered exposed to EMFs in this study was small. Two other studies have reported increases in risk of brain tumors with potential exposure among women, one of electricians and another of exposure to video display terminals. 22

The Shanghai Cancer Registry captures both malignant and benign tumors. Because risk factors for the two tumor types appear to differ, risks may actually be diluted from what we would see if we looked at results separately by histologic types. Information on occupation is for one moment in time—at tumor diagnosis for cases and at the time of the census for the comparison population. Having no information on job duration, we could not evaluated trends with duration. However, there is much less job mobility in China than in Western countries, particularly during the time period of the study, so this occupational information is likely to be fairly representative of usual occupation. Although the data for cases and the comparison population came from different sources, a study of a subsample of 400 men and women concluded that they had comparable and high accuracy.³ We evaluated brain tumor risk using and exposure assessment based on job titles. More detailed information on subjects' job histories would have made our exposure determinations more accurate. However, misclassification in this situation is likely to dilute associations.

In summary, we used data from the Shanghai Cancer Registry to identify occupational risk factors for brain tumors among women and to provide leads for future studies. Some results, such as those for farmers, rubber workers, and women with exposure to pesticides and organic solvents support previous findings that were based primarily on men. Our findings also indicate the need for further investigation of exposures that may be responsible for brain tumor excesses in nurses and textile workers.

References

- 1. Jin F, Devesa SS, Zheng W, Blot WJ, Fraumeni JF Jr, Gao YT. Cancer incidence trends in urban Shanghai, 1972–1989. *Int J Cancer*.1993;53:764–770.
- 2. Parkin DM, Muir CS, Whelan SL, Gao YT, Ferlay J, Powell J. Cancer Incidence in Five Continents. Vol VI. IARC Scientific Publication 120. Lyon, France: International Agency for Research on Cancer; 1992.
- Gao YT, McLaughlin JK, Gao RN, et al. Investigation of ocupational cancer incidence in Shanghai: background and methods. Shanghai Tumor. 1990;10:49– 53.

- Kneller RW, Gao YT, McLaughlin JK, et al. Occupational risk factors for gastric cancer in Shanghai, China. Am J Ind Med. 1990;18:69-78.
- Blair A, Zahm SH, Pearce NE, Heineman EF, Fraumeni JF Jr. Clues to cancer etiology from studies of farmers. Scand J Work Environ Health. 1992;18:209-215.
- Preston-Martin S, Lewis S, Winkelmann R, Borman B, Auld J, Pearce N. Descriptive epidemiology of primary cancer of the brain, cranial nerves and cranial meninges in New Zealand, 1948–1977. Cancer Causes Control. 1993;4:529–538.
- Musicco M, Filippini G, Bordo BM, Melotto A, Morello G, Berrino F. Gliomas and occupational exposure to carcinogens: case-control study. Am J Epidemiol. 1982;116:782-790.
- Musicco M, Sant M, Molinari S, et al. A case-control study of brain gliomas and occupational exposure to chemical carcinogens: the risk to farmers. Am J Epidemiol. 1988;128:778-785.
- Schlehofer B, Kunze S, Sachsenheimer W, Blettner M, Niehoff D, Wahrendorf J. Occupational risk factors for brain tumors: results from a population-based case-control study in Germany. Cancer Causes Control. 1990;1:209-215.
- Ronco G, Costa G, Lynge E. Cancer risk among Danish and Italian farmers. Br J Ind Med. 1992;49:220-225.
- Thomas TL, Waxweiler RJ. Brain tumors and occupational risk factors: a review. Scand J Work Environ Health. 1986;12: 1-15.
- Thomas TL, Stolley PD. Stemhagen A, et al. Brain tumor mortality risk among men with electrical and electronic jobs: a casecontrol study. J Natl Cancer Inst. 1987; 79:233-238.
- 13. Cordier S, Poisson M, Gerin M, Varin J,

- Conso F, Hemon D. Gliomas and exposure to wood preservatives. *Br J Ind Med.* 1988;45:705–709.
- Park RM, Silverstein MA, Green MA, Mirer FE. Brain cancer mortality at a manufacturer of aerospace electromechanical systems. Am J Ind Med. 1990; 17:537-552.
- Heineman EF, Cocco PL, Gomez M, et al. Occupational exposure to chlorinated aliphatic hydrocarbons and risk of astrocytic brain cancer. Am J Ind Med. 1994; 26:155-169.
- Gunnarsdóttir H, Rafnsson V. Cancer incidence among Icelandic nurses. J Occup Med. 1995;37:307–312.
- McLauglin JK, Malker HSR, Blot WJ, et al. Occupational risks for intracranial gliomas in Sweden. J Natl Cancer Inst. 1987;78:253-257.
- Ahlbom A, Norell S, Rodvall Y, Nylander M. Dentists, dental nurses, and brain tumors. *Br Med J [Clin Res]*. 1986; 292(6521):662.
- Englund A, Ekman G, Zabrielshi L. Occupational categories among brain tumor cases recorded in the cancer registry in Sweden. Ann NY Acad Sci. 1982;381: 188-196.
- Lin RS, Dischinger PC, Conde J, Farrell KP. Occupational exposure to electromagnetic fields and the occurrence of brain tumors. J Occup Med. 1985;27: 413-419.
- Mack W, Preston-Martin S, Peters JM. Astrocytoma risk related to job exposure to electric and magnetic fields. *Bioelectromagnetics*. 1991;12:57-66.
- Ryan P, Lee MW, North JB, McMichael AJ. Risk factors for tumors of the brain and meninges: results from the Adelaide adult brain tumor study. *Int J Cancer*. 1992;51:20-27.